

## Original Research Article

# Prevalence of *Helicobacter pylori* in children 2-16 years with chronic Idiopathic thrombocytopenic purpura referred to hematology clinic of Ardabil during 2013-2015

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## ABSTRACT

**Background:** Idiopathic thrombocytopenic purpura (ITP) is the most common autoimmune blood disorder which leads to premature destruction of platelets by producing antibodies using phagocytic cells against antigens of platelets surface especially in the spleen. Recently, several studies have reported the high prevalence of *H. pylori* infection in adult patients with chronic ITP, but the studies performed in this area have been very limited in children. The purpose of this study is to investigate the prevalence of *Helicobacter pylori* infection in children with chronic ITP.

**Methods:** In this case- control study, the case sample includes 30 children in the age range of 2-16 years with chronic ITP and control samples includes 90 children in the age range of 2-16 years who are healthy in terms of ITP disease. A questionnaire and a stool sample is prepared for each sample. These samples are examined by the method of ELIZA kit for the presence or absence of antigen *H. Pylori*. Data analyzed by statistical methods in SPSS.19.

**Results:** Of the total 30 children with chronic ITP who has referred to the haematology ward of the hospital, *H.pylori* + 16.7%, we had *H.pylori* + 20% from a total of 90 controls ( $P=0.68$ ). The average age of the case and control groups were  $6.9\pm2.8$  and  $6.9\pm3$  years, respectively; there is no a direct relationship between helicobacter pylori infection and sex, drinking water, but there is a statistically significant difference between platelet levels and the prevalence of *H Pylori* in the case group ( $p<0.05$ ); however, this difference is not significant in the control group.

**Conclusions:** According to a conducted study, *Helicobacter pylori* infection is not considered as a factor risk in the development of chronic thrombocytopenic purpura in children. So, it is recommended that further studies to be done in different ethnic groups in the world with more samples, especially in the age range of children, so that the role of *Helicobacter pylori* in the pathogenesis of chronic autoimmune thrombocytopenic purpura can be determined accurately.

**Keywords:** Chronic ITP, *H.pylori* infection, Platelet

## INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is the most common autoimmune blood disorder with different pathogenetic and clinical features in children and adults which determined through two mechanisms (produce antibodies against the platelets antigens by phagocytic

cells specialty in the spleen and early destruction of platelets.<sup>1-2</sup>

The prevalence of ITP in the United States of America were 50 cases, in Danish and UK 10-40 cases and in Kuwait more than 125 cases per one million people per year.<sup>3</sup>

Usually the disease occurs in children as thrombocytopenia, purpura, petechial rash, spontaneous bruising and mucosal bleeding (usually in the form of epistaxis) and divided clinically in two sections acute and chronic.<sup>4</sup>

In the acute form of the disease that is more common (70-80%), platelet count during the first 4 to 8 weeks and maximum up to 6 months returns to the normal level. The chronic form of disease refers to cases in which the platelet count between 6 and 12 months remain in less than 150 while the other causes of Thrombocytopenia not raised (including drugs, collagen scholar diseases and Hepatitis C, HIV) and hypoplasia of megakaryocytes level not seen in bone marrow aspiration.<sup>5-6</sup>

50-65% of patients with ITP have history of viral infection 1-4 weeks before and most of children have no symptoms in time of ITP incidence. Some vaccines such as triple vaccine and hepatitis B can cause disease incidence and in the spring, the acute type of ITP is more common. The relationship between *H. pylori* infection and ITP has been investigated since 1998 by an Italian group reported increase of the platelet count in ITP patients. The effect of *H. pylori* on the pathogenesis of immune destruction of platelets, is not yet clear. However, it was reported that treatment and extirpation infection in the children can increase the number of platelets which should be considered.<sup>7</sup>

*H. pylori* infection is usually acquired in childhood and remain for many years. The prevalence of *H. pylori* in childhood 10-80% and its highest prevalence were seen in developing countries. 80% of people infected with the bacterium are asymptomatic and in most children the infection didn't leads to clear clinical disease. Only 15% of infected children have clinical signs that this is affected by factors such as host, environment and bacteria.<sup>8</sup> The real infection rate among population in developing countries is more common and by increment age, poor economic and social conditions its prevalence rise.<sup>9</sup>

The prevalence of *H. pylori* infection in children with ITP varies widely among world's population. Generally, results of studies conducted on the ITP, showed that the prevalence of *H. pylori* infection in countries with high prevalence of infectious and autoimmune disease are more. Also, patients with ITP often are older than other patients. Given that *H. pylori* infection mainly occurs in childhood and could underline the prevalence of gastric cancer, peptic ulcer disease, ITP chronic and iron deficiency anemia, this study aimed to investigate the prevalence of *H. pylori* infection in children 2-16 years with chronic ITP.<sup>10</sup>

## METHODS

In this case control study, the case group included 30 children 2-6 years referred to Bu-Ali hospital that their

ITP previously approved by specialist and more that 6 months duration and the control group consisted of 90 children 2-16 years of healthy patient. Two case and control groups were matched in term of age, gender, and residence place, family history of blood and digestive diseases and nutritional habits.

After obtaining consent from parents for each of the samples a questionnaire was completed and a stool sample was taken of them. Children with platelet count less than  $100 \times 10^9$  per liter and without thrombocytopenia cause were studied. Children with a history of proton pump inhibitors, H2 blockers, and antibiotic uses within 4 weeks ago, liver disease, poor general health and artificial heart valves were excluded from study. After getting the stools, samples were studied by kite ELIZA (Enzyme-Linked Immunosorbent Assay) for the presence of antigen *H. pylori*. Collected data were analyzed using descriptive and analytical statistical methods in SPSS.16.

## RESULTS

Of the 30 ITP cases, 16 children (53.3%) were boy and 14 children (46.7%) were girl. In the control group 46 child (51.1%) were girl and 44 children (48.9%) were boy. The average age of children in case group was  $6.9 \pm 2.8$  age and in control group was  $6.9 \pm 3$  and the difference was not significant between the two groups. 30 children in the case group 5 children (16.7%) had *H. pylori* (20% girl and 80% boy) and of the 90 children in control group, 18 case (20%) had *H. pylori* (55.6% girl and 44.4% boy) and there was no difference between two groups (Table 1).

**Table 1: Rate of *H. pylori* in two groups.**

| Groups<br>Result of<br><i>H.pylori</i> test | Case |      | Control |     | p-value |
|---|------|------|---------|-----|---------|
|   | n    | %    | n       | %   |         |
| +   | 5    | 16.7 | 18      | 20  | 0.68    |
| -   | 25   | 83.3 | 72      | 80  |         |
| Total                                       | 30   | 100  | 90      | 100 |         |

Of positive cases with *H. pylori* in the study group, 9 people (30.3%) and in control group, 10 people (11.5%) had positive history of peptic ulcer in the family. The prevalence of *H. pylori* in control group is the same in every age group but the prevalence of *H. pylori* in case group in the age group 7 years and more was 17.6% of the age group of less than 7 years was 15.4% but the difference was not signification.

The patients with *H. pylori* in case group had platelet count less than 15000 and in the control group 16.7% had a platelet count less than 25000. There was a statistically significant difference between platelet levels and frequency of *H. pylori* in case group but there was no significant in the control group.

There was no significant correlation between household economic status and *H. pylori* infection in both groups. 71.7 % of the case group and 55% of the control group had taken from municipal water. In case group, 4 children (80%) with *H. pylori* and in the control group, 13 children (72.2%) with *H. pylori* used municipal water. It can be said that the higher prevalence of *H. pylori* was found in the stool of people had used the municipal and spring water but there was no significant difference between two groups.

## DISCUSSION

Till now many studies had been studied the possible role of infections (direct or indirect) in the occurrence of autoimmune diseases which can be pointed to the *H. pylori* microbe. Till now, many causes including viruses, vaccination, involvement of genetic factors and immune deficiency as the initiator production of auto antibodies in patients with ITP have been raised but in most cases the cause of the disease remains unknown. Firstly, Gasbarrini and colleagues considered *H. pylori* as a possible factor in occurrence of ITP. Although the mechanism by which *H. pylori* can be induced thrombocytopenia is still unknown.<sup>7</sup>

Several studies have been done on the prevalence of *H. pylori* in patients with chronic ITP especially in adults but because of unknown the exact rate of *H. pylori* in patients and also doing most of them in adults, doing other studies in this topic is necessary.<sup>8-10</sup> According to the study, infection with *H. pylori* infection in 30 children with a chronic ITP was 19.7% and in 90 healthy children with chronic ITP was 20% which wasn't statistically significant. In previous conducted studies, the rate of *H. pylori* in patients with chronic ITP was from 5.3% to 80%. In Company and Rezaei studies, *H. pylori* were seen in 8 persons of 40 children with ITP and 5 people of 23 children in the control group (17.4%) that the difference was no statistically significant between two groups and in line with our study result. In the Hamidieh and et al study, the mean age of patients was  $3.2 \pm 8.9$  years. Of all patients, 17 (54/9%) were female and 14 (45.1%) were male. The mean platelet count was  $34.3 \pm 51.4 \times 10^9$  (range from  $5 \times 10^9$  liters to  $125 \times 10^9$ ). The average duration of disease in the patients studied was  $20.2 \times 27.7$  (ranging from 7 to 96 months). Of patients only 4 children (21.9%) infected with microbe *H. pylori*. There was no significant correlation between gender and positive *H. pylori* antigen in two groups. In Azarm and et al study, significant difference between infected and non-infected patients mean age and gender distribution. The mean of platelet count in patients infected and non-infected in the baseline was  $3.5 \pm 3.7 \times 10^9$  liters and  $4.6 \pm 3.3 \times 10^9$  liters respectively and despite greater rate of chronic ITP disease in infected people, there wasn't relation between *H. pylori* infection and chronic ITP occurrence.<sup>11</sup> In Rajantie and et al study, there was statistically significant difference between platelet levels and frequency of *H. pylori* in case group

( $p=0.001$ ) but not in control group. Also, in Company study platelet count in patients with chronic ITP associated with *H. pylori* significantly lower than patients with chronic ITP but without the *H. pylori* infection ( $p < 0.05$ ) which was in line with our study results.<sup>12</sup>

In Vakili et al, study there was no statistically significant difference between infected and non-infected patients in terms of age, platelet count and duration of illness. Also, this study showed that the prevalence of *H. pylori* infection in children with chronic ITP is lower than adults. So, it can be concluded that *H. pylori* has not role in the occurrence of chronic ITP but in the kids deal to reducing platelets.<sup>9</sup>

In this study, the relationship between economic level and the test result was not significant which contradiction with Rahimian and et al study results but in line with Ghanei study.<sup>9,8</sup>

In the case of drinking water, the higher prevalence of *H. pylori* + in the stool of patients the urban water and spring water used in boiled water but a significant relationship between drinking water and infection in any of the cases group ( $p=0.88$ ) and control group ( $p=0.19$ ) was not observed is match with Rajantie study but not in line with Ghanei study.<sup>8,12</sup>

In compare, the results of this study with studies conducted in three countries Taiwan, Finland, Japan it

Was observed that the rate of *H. pylori* was 0%, 40.9% and 20%, respectively.<sup>13-15</sup>

Compare these three study together and also compare their results with current study because of difference in the prevalence of *H. pylori* infection in these countries and using different research methods, was different. It is essential to note that in our country due to indiscriminate use of antibiotics in children, self-elimination of *H. pylori* can reduce the prevalence of these bacteria. In most previous studies the prevalence of *H. pylori* was higher than our study considering the fact that most of these studies have been conducted in adult age group and infection with *Helicobacter pylori* increase with age and infection in adults is chronic and does not improve without any specific treatment.<sup>16-18</sup>

While in children, self-elimination (because of excessive use of antibiotics in children) can occur, compare frequency of *H. pylori* in patients with chronic ITP in two age groups (children and adults) is not correct. Accordingly compare of this study with other studies in Iran in adult age group was impossible.<sup>19,21</sup>

By comparing several studies conducted in adults with limited studies that have been conducted on children, were resulted that the prevalence of *H. pylori* in children with chronic ITP not as much as adults. Although *H.*

*pylori* in adults may be one of the causes of chronic ITP but does not seem to be similar in children.<sup>22-26</sup>

## CONCLUSION

The results showed that the prevalence of *H. pylori* infection in children with chronic ITP in compare with normal children was similar but platelet count in patients with chronic ITP along with *H. pylori* infection was significantly lower than patients with chronic ITP without *H. pylori* infection. It can be said that *H. pylori* infection does not lead to chronic ITP but in the children, deal to decline in platelets. So, doing future studies in different ethnic groups in the world with greater samples especially in children to exactly identification of *H. pylori* role in the pathogenesis of chronic ITP is recommended.

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